TEL: 9198622260

AUG 0 5 2004 JUNE AUGENABRY CHILLIAN

Appl. No.: 10/771,622 Filed: February 5, 2004 Page 2

## Amendments to the Claims:

## Claims 1-32 (Cancelled)

- 33. (New) A composite having a controlled rate of dissolution, said composite comprising:
- (a) a first region comprising calcium sulfate and at least one medicament, said first region exhibiting a first rate of dissolution; and
- (b) a second region comprising calcium sulfate and at least one medicament,
   said second region exhibiting a second rate of dissolution,

wherein said first rate of dissolution and said second rate of dissolution are different with respect to each other, and wherein said medicaments are selected from the group consisting of antibiotics, chemotherapeutic agents, growth factors, analysics, and combinations thereof.

- 34. (New) The composite of claim 33, wherein said first region and said second region each comprise at least one antibiotic.
- 35. (New) The composite of claim 34, wherein the at least one antibiotic in each region is selected from the group consisting of tetracycline hydrochloride, vancomycin, cephalosporins, aminoglycocides, and combinations thereof.
- 36. (New) The composite of claim 35, wherein the first region comprises tobramycin and the second region comprises gentamicin.
- 37. (New) The composite of claim 33, wherein said first region and said second region each comprise at least one chemotherapeutic agent.
- 38. (New) The composite of claim 37, wherein the at least one chemotherapeutic agent in each region is selected from the group consisting of cis-platinum, ifosfamide, methotrexate, doxorubicin hydrochloride, and combinations thereof.

TEL:9198622260

Appl. No.: 10/771,622 Filed: February 5, 2004 Page 3

- 39. (New) The composite of claim 33, wherein said first region and said second region each comprise at least one growth factor.
- 40. (New) The composite of claim 39, wherein the at least one growth factor in each region is selected from the group consisting of transforming growth factor beta (TGF-Beta), bone morphogenic protein (BMP), demineralized bone matrix (DBM), basic fibroblast growth factor, platelet-derived growth factor, and combinations thereof.
- 41. (New) The composite of claim 39, wherein at least one of said first region and said second region comprises a polypeptide growth factor.
- 42. (New) The composite of claim 39, wherein at least one of said first region and said second region comprises a bone morphogenic protein.
- 43. (New) The composite of claim 39, wherein at least one of said first region and said second region comprises demineralized bone matrix.
- 44. (New) The composite of claim 33, wherein said first region and said second region each comprise at least one analgesic.
- 45. (New) The composite of claim 44, wherein the at least one analysesic in each region is selected from the group consisting of lidocaine hydrochloride, bipivacaine hydrochloride, non-steroidal anti-inflammatory drugs, and combinations thereof.
- 46. (New) The composite of claim 45, wherein the non-steroidal anti-inflammatory drug is ketorolac tromethamine.
- 47. (New) The composite of claim 33, wherein at least one of said first region and said second region comprises demineralized bone matrix.

Appl. No.: 10/771,622 Filed: February 5, 2004

Page 4



- 48. (New) The composite of claim 33, wherein both said first region and said second region comprise demineralized bone matrix.
- 49. (New) The composite of claim 33, wherein at least one of said first region and said second region comprises demineralized bone matrix and at least one additional growth factor.
- 50. (New) The composite of claim 33, wherein said calcium sulfate of said first and said second regions is selected from the group consisting of alpha-calcium sulfate hemihydrate, beta-calcium sulfate hemihydrate, calcium sulfate dihydrate, or a combination thereof.
  - 51. (New) The composite of claim 33, wherein said regions are in the form of layers.
- 52. (New) The composite of claim 33, wherein said first region surrounds said second region.
- 53. (New) The composite of claim 33, wherein said calcium sulfate of said first region comprises calcium sulfate dihydrate prepared from alpha-calcium sulfate hemilydrate and said second composition comprises calcium sulfate dihydrate prepared from beta-calcium sulfate dihydrate.
- 54. (New) The composite of claim 33, wherein said calcium sulfate of said first region is prepared by contacting an alpha-calcium sulfate hemihydrate having a mean particle size in the range of about 12  $\mu$ m to about 23.5  $\mu$ m with an aqueous liquid.
- 55. (New) The composite of claim 54, wherein at least 80% of said alpha-calcium sulfate hemilydrate has a particle size in the range of about 12  $\mu$ m to about 22  $\mu$ m.

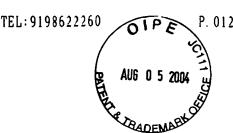
Appl. No.: 10/771,622
Filed: February 5, 2004
Page 5



TEL: 9198622260

- 56. (New) The composite of claim 54, wherein at least 80% of said alpha-calcium sulfate hemihydrate has a particle size in the range of about 16  $\mu$ m to about 22  $\mu$ m.
- 57. (New) The composite of claim 54, wherein from about 0.1% to about 2.0% of said alpha-calcium sulfate hemihydrate has a particle size of less than about 2  $\mu$ m.
- 58. (New) The composite of claim 54, wherein said alpha-calcium sulfate hemihydrate has a purity greater than 98 wt. % calcium sulfate hemihydrate.
- 59. (New) The composite of claim 54, wherein said alpha-calcium sulfate hemihydrate has a BET surface area in the range of about 0.2 m<sup>2</sup>/g to about 1.0 m<sup>2</sup>/g.
- 60. (New) The composite of claim 54, wherein said alpha-calcium sulfate hemihydrate has a density in the range of about 2.6 g/cm<sup>3</sup> to about 2.9 g/cm<sup>3</sup>.
- 61. (New) The composite of claim 54, wherein said calcium sulfate consists essentially of alpha-calcium sulfate hemihydrate having a purity greater than 98 wt. % calcium sulfate hemihydrate, a BET surface area in the range of about 0.35 m<sup>2</sup>/g to about 0.9 m<sup>2</sup>/g, a density in the range of about 2.73 to about 2.80 g/cm<sup>3</sup>, and a mean particle size in the range of about 16  $\mu$ m to about 22  $\mu$ m.
- 62. (New) The composite of claim 33, wherein said calcium sulfate of said first region is prepared by contacting calcium sulfate consisting essentially of beta-calcium sulfate hemihydrate having a mean particle size in the range of about 10  $\mu$ m to about 15  $\mu$ m with an aqueous liquid.
- 63. (New) The composite of claim 62, wherein said beta-calcium sulfate hemihydrate has a purity greater than 98 wt. % calcium sulfate hemihydrate.

Appl. No.: 10/771,622 Filed: February 5, 2004 Page 6



- (New) The composite of claim 62, wherein said beta-calcium sulfate hemihydrate 64. has a BET surface area in the range of about 5 m<sup>2</sup>/g to about 6 m<sup>2</sup>/g.
- (New) The composite of claim 62, wherein said beta-calcium sulfate hemihydrate 65. has a density in the range of about 2.5 g/cm<sup>3</sup> to about 2.6 g/cm<sup>3</sup>.
- 66. (New) The composite of claim 62, wherein said beta-calcium sulfate hemihydrate has a BET surface area in the range of about 4.5 m<sup>2</sup>/g to about 7.5 m<sup>2</sup>/g.
- 67. (New) The composite of claim 62, wherein said calcium sulfate consists essentially of beta-calcium sulfate hemihydrate having a purity greater than 98 wt. % calcium sulfate hemihydrate, a BET surface area in the range of about 4.5 m<sup>2</sup>/g to about 7.5 m<sup>2</sup>/g, a density in the range of about 2.5 to about 2.6 g/cm<sup>3</sup>, and a mean particle size in the range of about 13  $\mu$ m to about 14  $\mu$ m.
- 68. (New) The composite of claim 33, wherein the composite is in the form of a pellet.
- 69. (New) A composite having a controlled rate of dissolution, said composite comprising:
- (a) a first region comprising calcium sulfate and at least one medicament, said first region exhibiting a first rate of dissolution;
- (b) a second region comprising calcium sulfate and at least one medicament, said second region exhibiting a second rate of dissolution; and
- (c) one or more additional regions comprising calcium sulfate and at least one medicament, each of said one or more additional regions exhibiting a specific rate of dissolution,

wherein said first rate of dissolution, said second rate of dissolution, and each rate of dissolution of said one or more additional regions are different with respect to each other, and wherein said medicaments are selected from the group consisting of antibiotics, chemotherapeutic agents, growth factors, analgesics, and combinations thereof.

Appl. No.: 10/771,622 Filed: February 5, 2004 Page 7\_\_\_\_\_\_



- 70. (New) The composite of claim 69, wherein each region comprises at least one antibiotic.
- 71. (New) The composite of claim 69, wherein each region comprises at least one chemotherapeutic agent.
- 72. (New) The composite of claim 69, wherein each region comprises at least one growth factor.
- 73. (New) The composite of claim 72, wherein at least one region comprises a polypeptide growth factor.
- 74. (New) The composite of claim 72, wherein at least one region comprises a bone morphogenic protein.
- 75. (New) The composite of claim 72, wherein at least one region comprises demineralized bone matrix.
- 76. (New) The composite of claim 69, wherein each region comprises at least one analgesic.
- 77. (New) The composite of claim 69, wherein each region comprises demineralized bone matrix.
- 78. (New) The composite of claim 69, wherein at least one region comprises demineralized bone matrix and at least one additional growth factor.
- 79. (New) The composite of claim 69, wherein the composite is in the form of a pellet.

Appl. No.: 10/771,622 Filed: February 5, 2004 Page 8

ALSTON & BIRD



- 80. (New) A method of delivering a medicament to a mammal, comprising implanting the composite of claim 33 into the mammal.
- 81. (New) A method of delivering a medicament to a mammal, comprising implanting the composite of claim 69 into the mammal.